

Medical ethics and human subjects

In at least a dozen experiments humans have been subjected to questionable practices

The Tusgegee syphilis study went on for 40 years before public disclosure forced an investigation. Now the Department of Health, Education and Welfare has decided that the study was unethical, even when it started.

The sterilization of young girls in Alabama, while not a research project, is another case of questionable medical ethics. The Civil Rights Division of the Justice Department and the Senate health subcommittee are investigating charges that as many as 11 minors may have "undergone involuntary sterilization operations."

These highly publicized incidents "may give the erroneous impression that such procedures raising ethical questions are rare and involve only bizarre procedures. . . . This is not the case," say Robert M. Veatch and Sharmon Sollitto of the Institute of Society, Ethics and the Life Sciences in Hastings-on-Hudson, N.Y. In the June Report of the Hastings Center, they cite 11 studies they believe raise disturbing questions.

The studies were selected from a collection of 43 questionable experiments that have been published in responsible medical journals or professional proceedings since 1966. No names are mentioned but all the studies were performed in the United States or with funding from the United States.

The first three involved "grave risks to subjects." In one, nine normal female patients were given injections of epinephrine in an attempt to produce arrhythmia or abnormal heart beat. Those conducting the experiment admitted that such a procedure is hazardous, but they said, "informed consent cannot be obtained in a study of this type." In a second study, blood samples had to be taken from patients who had had both of their kidneys removed, some as recently as two weeks prior to the experiment. The ten subjects had to be transfused "in anticipation of blood loss due to repeated sampling." By the third day, "all subjects were clinically dehydrated." A third study involved giving LSD to 24 subjects in order to study long-range changes in personality, attitudes, values, interests and performance. No mention was made to the subjects of possible personality changes.

Four experiments involved risks to incompetent or incarcerated subjects. Nine children suffering from asthma were intentionally subjected to doses of

antigens known to produce asthmatic attacks. In another experiment, 48 children suffering from blood diseases were subjected to dual-site bone marrow withdrawals. The study pointed out that such procedures "involve physical and psychological problems" for children.

In prisons or mental institutions, the quality of consent, even if it is obtained, is questionable. At a maximum security facility for the criminally insane, 90 patients were "used in an exploratory study to determine the effectiveness of succinylcholine as an agent in behavior modification." The drug causes temporary muscle paralysis, including inability to breathe.

Another experiment in operant conditioning was reported by an American psychiatrist working at a mental hospital in Vietnam. Chronic male patients (mostly schizophrenic) were offered freedom if they proved they could work. Of 130, only 10 volunteered to work. The rest were told they needed treatment and were given electroconvulsive shock. After a few treatments, most of the men decided to work. A similar experiment was then tried on 130 women. Even after each had received 20 treatments, only 15 were willing to work. Shock treatments were discontinued and food was withheld for periods of up to three days. The patients were eventually cured and went to work tending crops for the Green Berets.

In a placebo experiment, 91 of 130 children with bronchial asthma received injections of buffered saline instead of medication. This ineffective treatment lasted in some cases for 14 years. Neither the children nor their parents knew an experiment was going on. In an experimental birth-control program, 262 women had megestrol acetate capsules implanted in their forearms to test the long-term contraceptive effectiveness of the drug. This experiment produced 48 unwanted pregnancies. In a study involving legal and psychological risks, 332 patients in a voluntary psychiatric hospital were subjected to urine analysis for drug use. No consent was obtained and the patients did not know what the test was for. In a final experiment, 41,119 patients enrolled in a group health plan were given a test for pain tolerance as part of their regular checkup. They were subjected to as much pain as they could stand but did not know they were

part of an experiment.

These examples, say Veatch and Sollitto, indicate the need for mechanisms for consent and review which give greater assurance that the rights and interests of subjects will be protected. The procedures now available, they say, are inadequate. In peer review, for instance, it is the peers of the researchers not the peers of the subjects who are asked to evaluate the ethical acceptability of the proposed research. Conclude the Hastings Center researchers: "The immediate establishment of a governmental committee to formulate rigorous procedures to ensure reasonable informed consent and review is the minimum that is called for."

This week, after testimony from the family involved in the Alabama sterilization case, the Senate health subcommittee began consideration of a bill that would strictly control medical experimentation. In a similar case, judges in Detroit ruled this week that psychosurgery may not be performed on prisoners or mental patients confined against their will. □

Infant mortality in the

In spite of the United States' high standard of living and medical sophistication, newborn death rates are shamefully high. And they are getting worse. Several years ago 13 countries had lower infant death rates than the United States. Now 15 countries do.

The Institute of Medicine of the National Academy of Sciences has now issued a study that offers unprecedented insights into the causes of deaths among American newborns. The study is based on records of 140,000 births in New York City in 1968. It relates demographic, social and medical factors to differences in the medical services needed and received by pregnant women. The study was headed by David M. Kessner, professor of community medicine at Georgetown University.

The study's findings underscore the marked influence of social risks, medical risks and prenatal care on infant survival. Social risks include minimal education, having many

A third hormone that can induce mating

A few years ago, endocrinologists isolated and synthesized a little-known hormone found in the brain's hypothalamus that controls the release of luteinizing hormone (LH), hence its name luteinizing release factor (LRF). LH causes the secretion of estrogen and progesterone and the onset of ovulation. It has been shown that the combination of estrogen and progesterone affects sexual behavior in subprimate female mammals.

Now scientists in Dallas have made a further step forward in understanding the many roles hormones play in sexual behavior. They have found that if LRF replaces progesterone, in the estrogen-progesterone combination, mating behavior is induced in female rats whose ovaries have been removed.

Physiologists S. M. (Don) McCann and Robert L. Moss of the University of Texas' Southwestern Medical School performed experiments on ovariectomized female rats to determine whether the preovulatory discharges, LRF, FSH (follicle-stimulating) and LH might also be involved in the induction of mating behavior.

Eighteen such rats were injected with low dosages of estrogen and placed in one of six experimental groups. Groups consisted of rats with estrogen only, rats with estrogen and progesterone and rats with estrogen and one of

four other hormones: LRF, LH, FSH and TRF (thyrotropin-releasing factor).

Those injected with estrogen alone, estrogen and FSH, estrogen and LH and estrogen and TRF showed little response to the presence of a male. As expected, all animals treated with estrogen and progesterone displayed sexual behavior 48 hours after injection.

The most dramatic results were obtained in the females treated with estrogen and LRF. Two hours after injection, signs of female sexual behavior began. Male rats could induce coitus behavior in females for at least six hours.

"The results are of extreme interest," says Moss in the July 13 *SCIENCE*, "since they indicate that another hormone in addition to estrogen and progesterone can induce mating behavior in the female rat. Particularly intriguing is the fact that this hormone is normally found in that area of the nervous system which is involved in mediating mating. It will be of extreme interest to determine if LRF can enhance mating behavior in males as well as in females. . . ."

The results of the experiments may prove to be even more important if further experimentation shows LRF can affect copulation in humans. LRF may be helpful in the treatment of impotence in males where no organic defect can be found. It may also become useful as a cure for frigidity and infertility in women. LRF is non-toxic in humans and has already been used to increase LH production. □



U.S. Geological Survey

Eruption of Nicaragua's Cerro Negro.

Volcano forecasting: Imprecise but improving

The awesome forces of nature are dramatically expressed by volcanoes. Active volcanoes in Mexico and Central America are major geologic features in those regions, and their eruptions tend to be highly explosive. What are the chances of forecasting the eruptions?

"The state of the art of volcano forecasting is far from precise," Robert

United States: A study of 140,000 births emphasizes prenatal care

children already, being unwed or without male support. Medical risks include diabetes, high blood pressure or toxemia of pregnancy.

If women were at neither social nor medical risk and received adequate care during pregnancy, deaths among their newborns, the study found, were 13 per thousand. This rate approaches that of the Scandinavian countries, which is among the lowest in the world. If women received adequate care but were at either medical or social risk, deaths among their babies were 24 per thousand, about twice as high. If women received adequate care but were at both medical and social risk, deaths among their offspring were 36 per thousand, or three times as high. If women were at no risk but received poor care, deaths were 30 per thousand. If women were at social risk and received poor care, deaths were 46.4 per thousand. And if women were at both social and medical risk and received poor care, deaths were

55.1 per thousand.

Seventy percent of the women with risks received poor care. Sixty percent of the women without risks received adequate care.

Most of the women at risk and getting bad care were black and Puerto Rican. Of some 22,000 black and Puerto Rican mothers at social risk, 98 percent received inadequate care. By contrast, white mothers were generally without risk and received adequate care. White women with no risks and good care had death rates of nine per thousand.

The most surprising result of the study, in Kessner's view, is the impact of prenatal care on infant survival. Because infant deaths were highest among blacks, Puerto Ricans and other people in the inner city, the report addresses its recommendations largely to health care centers in the inner city. These include some 75 neighborhood health centers, formerly under the Office of Economic Opportunity and now under Health, Education and Welfare, plus family

health centers at teaching hospitals in various cities.

The prime recommendation is that women be screened for social and medical risks on their first visit to a center. Says Kessner, "Ninety-five percent of all the women we studied had risks that could have been identified at the first prenatal visit." Then those women with identified risks should receive special attention throughout their pregnancies. Their newborns should also be put in neonatal intensive care units.

The report also recommends that the American College of Obstetricians and Gynecologists establish guidelines for maternal health care appropriate to risk categories, and that minimum-care standards be incorporated in existing Federal, state and local programs for maternal health care.

If all the women in the New York City study had received adequate care, infant deaths could have been reduced a third—from 21.9 per thousand to 14.7.